939-78 Selective Angiotensin II Receptor Antagonism Does not Influence Myocardial Stunning but Augments Ischemic Pre-conditioning in the Pig Heart

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The effects of a new angiotensin II receptor antagonist (EXP 3174, an active carboxylic acid analog of the selective angiotensin II receptor antagonist DuP 753) on infarct size and regional contractile function in an open-chest pig model of ischemia and reperfusion were evaluated. Ischemic preconditioning (PC) was performed by twice 10 min LAD occlusion (CO) and 30 min reperfusion (RP) followed by 1 hour CO and 1.5 hour RP. Infarct size (IS) in the left ventricle in % of risk area (RA) was determined by tetrazolium salts and regional segment shortening (%SS) by subendocardial implanted ultrasonic crystals in the LAD supplied area. Group (Gp) 1 = control (1 h CO + 1.5 h RP), Gp 2 = control + EXP 1 mg/kg iv, Gp 3 = PC, Gp 4 = PC + EXP 0.3 mg/kg iv, group 5 = PC + EXP 1 mg/kg iv. %SS after PC was 22.2 ± 7.2 in Gp 3, 19.9 ± 0.9 in Gp 4, and 17.1 ± 4.5 in Gp 5 ($p > 0.05$).

Gp	n=	RA/LV (%)	IS/RA (%)
1	5	16.1 ± 2.2	71.3 ± 3.8
2	4	22.3 ± 3.3	57.5 ± 3.1
3	7	16.9 ± 1.3	36.5 ± 4*
4	4	15.9 ± 3.8	40.3 ± 5.2*
5	5	13.6 ± 6.3	6.7 ± 3.1**

LV = left ventricle, *$p < 0.05$ vs Gp 1, ** vs Gp 3

Administration of EXP 3174 neither alters IS in controls nor %SS after brief periods of ischemia, however, IS after PC are dosedependent significantly reduced, indicating a supportive role of angiotensin II receptor activation for infarct size limiting effects of ischemic preconditioning in our pig model.

939-79 Role of Collateral Circulation in Protection Afforded by Regional Ischemic Preconditioning to Remote Myocardium

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Repeated brief circumflex (CX) coronary artery occlusions precondition (PC) the left anterior descending (LAD) coronary artery bed in dogs. The mechanism of this protection might be due to transportation, via coronary collaterals, of catabolites produced during ischemia/reperfusion (like adenosine) from the CX bed into the LAD bed. We sought to determine whether this protection might apply to species lacking collateral circulation. Twenty-eight pigs underwent 40 min of LAD occlusion and 2 hours of reperfusion. Prior to this they underwent a 20 min treatment period consisting of either no intervention (control; n = 9), 10 min LAD occlusion/10 min LAD reperfusion (LAD-PC; n = 12) or 10 min CX occlusion/10 min CX reperfusion (CX-PC; n = 7). Area at risk and infarct size were measured by injection of blue dye and triphenyltetrazolium staining, respectively. All three groups had similar area at risk (expressed as % of the LV weight) that averaged 17 ± 6%, 17 ± 3% and 18 ± 4% in the control, LAD-PC and CX-PC groups, respectively (p = NS). As expected, infarct size (expressed as % of the area at risk) was significantly reduced in the LAD-PC group: 9 ± 14%* vs 53 ± 19% in the control group (*$p < 0.05$). In contrast, CX-PC pigs did not display any infarct size limitation: 44 ± 15% vs 53 ± 19% in controls (p = NS). This demonstrates that preconditioning the circumflex bed does not protect the remote LAD myocardium in pigs, and further suggests that the beneficial effect reported in dogs might be partly due to circulation of some mediator throughout the heart via collateral vessels.

939-80 Quantitative Three-Dimensional Echocardiographic Estimation of Ischemic and Non-ischemic Myocardial Mass and its Relation to the Mass of Dysfunctional LV Myocardium During Coronary Occlusion

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While measurement of non-perfused LV mass is possible in autopsied hearts with pre-injected radionuclide agents, *in vivo* measurement of the mass of ischemic (ISC) myocardial (M) regions has not been feasible. 2D echo with contrast depicts ISC regions but does not provide 3-dimensional mass of these regions. Advances in volume-rendered 3D echo (3DE) provide an opportunity to estimate not only global but also regional LV mass. 3DE's ability to measure LV mass has been validated. In this study, we evaluated the relation between ISC M mass and the mass of dysfunctional M using a newer ultrasound contrast agent FS069 (MBI) that provides prolonged contrast effect. In 7 dogs, 3DE was performed with computer-controlled sequential scanning, at baseline and following aortic root injection of FS069. Baseline and contrast data were acquired in the control state and following occlusion of the LAD, PDA and OM coronary artery branches (10 occlusions). From volume-rendered 3DE, we were able to extract ISC (contrast defects) and non-ISC regions and measure the myocardial volume of these regions without any geometric assumptions. Multiplication by M density yielded M mass of the ISC, non-ISC and whole M. From dynamic 3DE, we were also able to demarcate the region of dysfunctional M in all dimensions, and measure its mass. The extracted ISC territories when visualized in 3 dimensions from different orientations appeared as curved M walls of various shapes and sizes, depending on the amount of ischemic M. The location, size and geometry of the hypoperfused regions corresponded well with those of dyssynergic zones. The mass of non-perfused M in the 7 dogs was 13.9 ± 8 grams (range 3.6–26.3) representing 18 ± 9% of total LV mass. The mass of abnormally contracting M, calculated independently, was 12 ± 7.4 g (range 0–21), or 17 ± 10% of the whole LV. There was an excellent correlation between the ischemic mass (x) and dyssynergic mass (y), $y = 0.114x + 0.85$, $r = 0.92$ $p < 0.001$. *Conclusion:* Using volume-rendered 3D Echo, the actual mass of ischemic and non-ischemic M regions and its relation to dysfunctional M can be defined and quantified. Such a quantitative 3DE approach may assist in the studies of ischemia, thrombolysis and reperfusion.

939-81 Thrombolysis Enhanced by Ultrasound on Intracoronary Thrombus

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The synergistic effect of combined usage of ultrasonic irradiation and t-PA was examined on intracoronary thrombus, produced in the canine left anterior descending artery (LAD). t-PA was given as a bolus dose of 0.1 mg/kg followed by an infusion of 0.9 mg/kg in one hour, until recanalization (TIMI 2). Canines were randomly divided into two groups, one of which (n = 5) received continuous ultrasonic irradiation (200 kHz, 0.25W/cm^2) directly to the LAD occluded by thrombus. The other group (n = 4) served as the unirradiated control. Ultrasonic irradiation significantly reduced both the time required for recanalization (irradiated 13.6 ± 6.0 min. vs. control 36.0 ± 18.0 min.; $p < 0.05$) and the administered dose of t-PA (0.32 ± 0.11 mg/kg vs. control 0.64 ± 0.27 mg/kg; $p < 0.05$). Upon electron microscopical examination, ultrasonic irradiation had no damage on the tissue morphology. This simple method safely could enhance the thrombolytic effect of t-PA and could make rapid coronary recanalization and reduction the dose of t-PA. We expect this method may be applied to the treatment of acute myocardial infarction.

939-82 Efficacy of Gadolinium-BOPTA in Magnetic Resonance Imaging to Assess Acute Myocardial Infarction in Man

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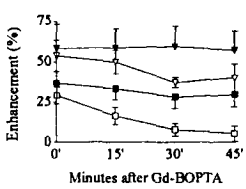
To assess the efficacy of the newly developed contrast agent gadolinium (Gd) benzyloxy propionic tetraacetic-acid BOPTA to detect acute myocardial infarction in patients using magnetic resonance imaging (MRI), 24 patients (age 53.3 ± 8.3) were examined 9.3 ± 3.7 days after a first myocardial infarction. Short axis T1 weighted images were obtained at 3 slice levels, before, immediately after injection of Gd-BOPTA, and after 15 min, 30 min, 45 min. Patients were divided into 2 groups according to the dose of Gd-BOPTA (0.05 mmol/kg and 0.1 mmol/kg). Contrast to noise ratio, signal intensity enhancement of normal and infarcted myocardium and signal intensity of infarcted to signal intensity of normal myocardium (SI inf/norm) was quantified. Contrast to noise ratio was not affected by the type of dosage (0.05 mmol/kg, 5.75 ± 0.85 vs. 0.1 mmol/kg, 5.32 ± 0.69). Enhancement of normal and infarcted myocardium increased immediately after administration of 0.05 mmol/kg Gd-BOPTA and gradually decreased thereafter ($p < 0.002$ for normal myocardium) (see Figure). After 0.1 mmol/kg Gd-BOPTA administration, myocardial enhancement increased rapidly but showed no decrease within 45 minutes after administration (see Figure). Mean SI inf/norm was significantly improved after Gd-BOPTA ad-



ministration ($p < 0.0005$ for either dosage), and 0.05 mmol/kg produced significantly higher SI inf/norm than 0.1 mmol/kg (1.42 ± 0.069 vs. 1.34 ± 0.055 respectively, $p = 0.015$). *Conclusion:* Gd BOPTA is a useful contrast agent to assess myocardial infarction. Optimal results are obtained with a dosage of 0.05 mmol/kg body weight Gd-BOPTA. Persistent enhancement of infarcted and normal myocardium suggests an affinity of Gd-BOPTA for myocytes, making it a promising tool in MR imaging of ischemic heart disease.

940 Myocardial Infarction — Reperfusion

Tuesday, March 21, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

940-71 Relative Importance of Acute Left Ventricular Function, Infarct Artery Patency, and Improvement of Left Ventricular Function for Late Survival After Direct Angioplasty for Acute Myocardial Infarction

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Of 663 pts with acute infarction treated with direct angioplasty, 576 hospital survivors were followed 5.3 yrs (median). Late ejection fraction (EF) data were obtained in 54% of pts at 6–8 mos. There were 48 late cardiac and 37 non-cardiac deaths. Late infarct related artery (IRA) patency was 92%. Multivariate predictors of late cardiac mortality by Cox regression were acute EF ($P = 0.0001$), improvement in EF ($P = 0.0001$), prior bypass surgery ($P = 0.005$), and female gender ($P = 0.05$). Late survival was excellent in pts with acute EF $\geq$ 45% vs pts with acute EF < 45% (7 yr survival 89% vs 71%, $P = 0.004$). Patency of the IRA was not a significant predictor of late survival in pts with acute EF $\geq$ 45%, but was a significant univariate predictor in pts with acute EF < 45% (6 yr survival patent vs occluded: 89% vs 35%, $P = 0.004$). Patency was important for improvement of left ventricular function (LVF) (late improvement in EF in patent vs occluded IRA: + 4.8% vs − 4.8%, $P = 0.001$). Although patency was important for survival in pts with depressed LVF by univariate analysis, in a multivariate model which included both patency and improvement in EF, only improvement in EF was a significant independent predictor ($P = 0.0001$).

Conclusion: Acute LVF is the most important determinate of late survival. IRA patency is important for late survival in pts with depressed acute LVF, but this appears to be related to its effect on improvement in LVF rather than through an independent effect.

940-72 Effect of Late Coronary Angioplasty of an Infarct-related Vessel on Left Ventricular Function

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Conflicting results regarding a possible beneficial effect of *late* percutaneous transluminal coronary angioplasty (PTCA) of an infarct-related vessel on left ventricular function have been reported. These discrepancies may be related to relatively low numbers of patients, to the heterogeneous nature of the populations studied, to low sensitivity of the technique used to detect changes in LV function, or to incomplete follow-up. We studied 100 consecutive patients who had successful PTCA of a left anterior descending artery lesion $\geq$1 month after an anterior myocardial infarction (MI) and who underwent systematic angiographic follow-up 6 months later. TIMI flow pre-PTCA was <3 in 30% of the patients. The parameters of LV function assessed pre-PTCA and at 6 months using quantitative angiography were ejection fraction (EF), end-diastolic volume index (EDVI), end-systolic volume index (ESVI), and segmental wall motion in five segments of the anterior wall (SWM1 through 5).

	Before PTCA	Follow-up	
EF (%)	53.3 ± 15.4	53.8 ± 13.7	NS
EDVI (ml/m^2)	92.9 ± 22.8	96.4 ± 27.7	NS
ESVI (ml/m^2)	44.2 ± 21.7	46.2 ± 24.6	NS
SWM1 (%)	33.3 ± 16.6	34.8 ± 15.3	NS
SWM2 (%)	25.7 ± 25.2	26.5 ± 26.5	NS
SWM3 (%)	21.1 ± 29.2	21.8 ± 32.2	NS
SWM4 (%)	18.6 ± 29.3	17.6 ± 32.7	NS
SWM5 (%)	12.4 ± 25.7	14.0 ± 25.9	NS

Conclusion Whereas direct PTCA for acute MI has a documented beneficial effect on LV function, our results demonstrate that PTCA of an infarct-related lesion performed more than 1 month after the MI is not associated with any long term improvement in LV function.

940-73 Predictive Value for Major Arrhythmic Events of Ventricular Arrhythmias Detected in the Subacute Phase of a Fibrinolysed Myocardial Infarction. An Analysis of the GISSI-2 Data Base

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The relationship between ventricular arrhythmias (VA) in the subacute phase of a myocardial infarction and subsequent major arrhythmic events (MAE) was mainly defined in the prefibrinolytic era. We examined the large population of patients enrolled in the GISSI-2 study in order to evaluate the significance and predictive power for MAE (sustained ventricular tachycardia -SVT- and sudden death -SD-) of VA detected by Holter monitoring during the subacute phase of a fibrinolysed acute myocardial infarction (AMI). Of the 12,381 pts. enrolled in the GISSI-2 study, an Holter monitoring was available in 8,676 and a six month follow-up was completed in 7,713. During the follow-up 84 pts. died suddenly and 26 experienced one or more SVT. The relationship between VA and MAE was evaluated by odds ratio (OR) and their 95% confidence intervals. OR for MAE was 4.5 (2.7–7.5) if the Holter showed >10 ventricular ectopic beats per hour; 2.3 (1.5–3.7) if couplets were present; 3.3 (1.5–7.0) if nonsustained ventricular tachycardias (NSVT) were noticed; 3.0 (2.0–4.5) if any complex VA was detected. A multivariate analysis (Cox model) including the major prognostic determinants confirmed the independent prognostic value of VA in the Holter recording except for NSVT. Any arrhythmic parameter had a very low positive predictive power (from 2.4 to 3.0%). In conclusion, our data show that VA still have, in the fibrinolytic era, a prognostic significance for MAE, but the predictive power is very low and is therefore mandatory to add other variables to identify the pts. more at risk.

940-74 Spontaneous Delayed Reperfusion of Infarcted Area Limits Progressive LV Remodeling After Anterior Q-Wave MI

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We recently documented that perfusion and contraction in the infarct zone improve after the first 5 weeks after MI in a substantial percentage of pts (delayed reperfusion), suggesting a period of hibernation after acute MI. Although early reperfusion is known to prevent LV remodeling, it is unknown whether this delayed (>5 weeks) spontaneous reperfusion has any effect on progressive LV remodeling. Thus, we evaluated prospectively 79 consecutive pts (50 ± 8 years; thrombolysis in 58 pts) 5 weeks and 7 months after a first uncomplicated Q-wave anterior MI. Resting regional contraction and perfusion were serially evaluated by quantitative 2D-echo and Sestamibi tomography. At 5 weeks, all pts had significant (>2SD normal values) wall motion abnormalities (WMA) and perfusion defects in the infarcted area.

A significant (>95% reproducibility limits) improvement of perfusion in the infarcted area was documented at 7 months in 50 pts (63%, REP) while perfusion was unchanged/worsened in 29 pts (noREP). At 5 weeks, the extent of perfusion defect and WMA in the infarcted area, EF, end-diastolic volume index (EDVi, ml/m^2), regional dilation (RDIL) and expansion index (EXP) were comparable between REP and noREP.

At 7 months, noREP pts showed increased EDVi (66 ± 14 vs 70 ± 18, $p < 0.05$), a slight increase in RDIL (27 ± 25% vs 32 ± 30%, NS), with unchanged WMA (37 ± 14% vs 36 ± 17%), EF (45 ± 12% vs 46 ± 13%) and EXP (1.1 ± 0.1 vs 1.1 ± 0.3). In contrast, REP pts showed no changes in EDVi (60 ± 15 vs 61 ± 18) and RDIL (21 ± 21% vs 21 ± 26%) and improvement in WMA (31 ± 15% vs 26 ± 20%, $p < 0.05$), EF (51 ± 13% vs 55 ± 14%, $p < 0.01$) and EXP (1.1 ± 0.1 vs 1.0 ± 0.4, $p < 0.05$). The results suggest, for the first time, that spontaneous reperfusion occurring as late as >5 weeks after anterior Q-wave MI can limit the degree of LV remodeling at 7 months. This raises the possibility that delayed (>5 weeks) interventional recanalization may be beneficial in pts with persistent perfusion defects after acute MI.

940-75 Effect of Coronary Revascularization on Left Ventricular Remodeling in Patients Receiving Thrombolytic Therapy for Myocardial Infarction: A One Year Follow-up

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Remodeling starts in the acute phase of myocardial infarction by infarct formation and expansion. Thrombolytic therapy in the acute phase may affect infarct formation. Whether coronary revascularization (CR) in the subacute or chronic phase may add to the prevention of dilatation is not known. In a post-hoc analysis, we investigated the effect of coronary angioplasty (PTCA) and coronary bypass surgery (CABG) on left ventricular volume assessed by serial echocardiography during a one year follow-up.